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10/517,684	06/06/2005	Kathleen Grace Mountjoy	BSWV-P01-007	3069

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FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,684	MOUNTJOY ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-20,23,25 and 29-34* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11,14-20, 23, 25, 29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6 March 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group V, claims 9-11, 14-15 (in part), 16, 17-20 (in part), 23, 25 (in part), 29-33 (in part) and new claim 34 in the reply filed on 20 February 2007 is acknowledged. The traversal is on the ground(s) that the restriction requirement only argued that Groups IV-VII do not share the same special technical feature with Group I, but that they do share the same special technical feature with each other. This is not found persuasive because the instant case was filed under 35 U.S.C. 371, thus the decision of lack of unity is made by comparison of the first claimed invention and the subsequent inventions, and not between each invention individually (as is the case in applications filed under 35 U.S.C. 111). Although the Groups IV-VII have some method steps in common, they do not share a special technical feature with Group I, the first claimed invention, thus unity of invention is broken for the claims as a whole. Furthermore, art was applied to the claims (see below under Rejections under 35 U.S.C. 102(b)), thus there is no special technical feature that distinguishes over the prior art. Upon further consideration, however, Group IV, drawn to claims 8, 14-15 (in part), 17-20 (in part), 23, 25 (in part), 29-33 (in part) contain the same method steps, and will rejoined with Group V. Thus claims 8, 9-11, 14-15, 16, 17-20, 23, 25 and 29-34 will be examined insomuch as they are drawn to methods of assessing feeding, weight gain or assessing, diagnosing or predicting risk in a subject comprising measurement of two melanocortin peptides in a sample obtained from said subject and comparison of the ratio with a reference value.

In addition, it is noted that Applicants elect proteins involved in the melanocortin peptidergic axis in the species election requirement.

The requirement is still deemed proper and is therefore made FINAL.

Claims 12-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 20 February 2007.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 9-11, 14, 16, 17-20, 23, 25 and 29-31, 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. First, the claims recite methods for assessing feeding and/or weight gain, predicting risk, diagnosing obesity and/or energy imbalance in an individual comprising measurement of at least two melanocortin peptides in a sample, calculating the ratio, and comparing the value of the ratio with a reference value, but do not recite what the comparison is supposed achieve, thus the method steps do not complete the goal of the preamble, i.e, assessing feeding and/or weight gain, predicting risk, diagnosing obesity and/or energy imbalance. The omitted steps are a positive recitation of what the comparison step achieves. Second, no particular patient population is specified in the claims, thus for

the purpose of prior art, the broadest reasonable interpretation of the claims is the measurement two melanocortin peptides in a sample, calculating the ratio, and comparing the value of the ratio with a reference value in any patient population for any purpose. Note that a clear recitation of what the steps achieve and the patient population targeted would obviate this rejection.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-11, 14-15, 16, 17-20, 23, 25 and 29-30, 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for assessing feeding and/or weight gain, predicting risk, diagnosing obesity and/or energy imbalance in an individual at risk for energy imbalance and/or obesity comprising measurement of α-MSH and desacetyl-α-MSH in a sample, calculating the ratio between desacetyl-α-MSH and α-MSH, and comparing the value of the ratio with a reference value, wherein a higher desacetyl-α-MSH/α-MSH ratio in the sample is predictive of a risk of energy imbalance and obesity, does not reasonably provide enablement for the claims as broadly recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

First, neither the specification nor the literature suggests that the ratio of any two melanocortin peptides could be used to predict risk, diagnose obesity and/or energy imbalance in a subject. On the contrary the instant specification clearly indicates (see p. 19, lines 1-9) that it is the ratio of desacetyl-α-MSH/α-MSH as measured in plasma that predicts risk, not any two melanocortin peptides. The state of the art demonstrates a great deal of unpredictability in the literature with regard to the instant invention. The literature teaches that peripherally administered desacetyl-α-MSH and α-MSH influence postnatal rat growth (Wu et al., Am J Physiol Endocrinol Metab. 2006; 291: E1372-E1380; abstract; Mauri et al. Regulatory Peptides. 1995; 59-66; abstract); that a 9 year old female having early onset obesity presented with elevated levels of proopiomelanocortin (POMC—see Jackson et al. J Clin Endocrinol Metab. 1999; 84: 819-820; whole document—on Applicants 1449 form); that exogenously administered α-MSH and β-MSH reduce food intake, and that higher doses of desacetyl-α-MSH also

reduce food intake, but that γ_2-MSH has no effect on food intake in fasted rats (Abbott et al. Brain Research. 2000; 869: 203-210; abstract); that desacetyl-α-MSH stimulates lipid mobilization in the rainbow trout, but not α-MSH, β-MSH or β-endorphin (Yada et al. Zoological Science. 2000; 17: 1123-1127; p. 1124, Fig 1); that ***β-MSH*** and ***not α-MSH*** is the endogenous ligand that inhibits food intake (Harrold et al. Peptides. 2003; 24: 397-405; p. 404, left column, last paragraph); that elevated plasma levels of α-MSH are correlated with insulin resistance in obese males (Katsuki et al.; International Journal of Obesity. 2000; 24: 1260-1264; abstract—on Applicants' 1449 form); alternatively that elevated hypothalamic levels of ***agouti-related protein (AGRP) but not α-MSH or POMC*** may indicate obesity or energy imbalance (Harrold et al. Biochem Biophys Res Commun. 1999; 258: 574-577—on Applicants' 1449 form) and finally, that peripheral α-MSH may promote lipogenesis (i.e. producing fat) in ungulates (Am J Physiol Regulatory Integrative Comp Physiol. 2001; 281: R76-R90—on Applicants 1449 form). Not only do the findings in the literature not support the claims that any two melanocortin peptides could be used, but the person of skill in the art could not predict which two melanocortin peptides could be measured in the instantly claimed methods to predict risk, diagnose obesity and/or energy imbalance. Given the state of the art and the unpredictability of the art, the issue of determining which two melanocortin peptides could be used in the instantly claimed methods is a complex one, i.e., there is little agreement or guidance in the literature. When there is a lack of guidance in the literature, the person of skill in the art must rely on the teachings of the specification, and the specification teaches only ***an elevation*** in the ratio of desacetyl-α-MSH/α-MSH

predicts risk, not any two melanocortin peptides or any ratio. Establishing a method for predicting risk using other melanocortin peptides would result in undue experimentation, and furthermore, the breadth of the claims as instantly written would unfairly stifle further research in the area of melanocortins in energy research. Given the unpredictability of the art and what the specification teaches and does not teach and the breadth of the claims, the person of skill in the art would not be able to predict what other melanocortins (besides those taught in the specification) could be used in the instantly claimed invention. Furthermore, regarding claims 15 and 33, "the profile of response parameters" is defined at p. 13 of the instant specification in the following way: "includes a cellular product which may be a protein, nucleic acid, lipid, carbohydrate or a combination of these), or a measurable cellular event resulting from an interaction of the biological response system with a melanocortin peptide, for example cell proliferation, cell cycle progression, cell differentiation and the like, mass spectrometry or currently commercially available gene expression arrays may be used to monitor these response parameters, among other techniques. Given the lack of predictability in the art discussed above, only proteins involved in the melaocortin peptidergic axis would be informative with regard to predicting risk or diagnosing obesity and/or energy imbalance in the instantly claimed methods invention.

Furthermore, claim 15 recites "measured by a biological response system", which is defined in the specification at p. 13 as "any whole animal, organ, tissues or cell which is able to respond to a melanocortin peptide or an effector molecule generated by a response to a melanocortin peptide," which given the unpredictability in the art and the

lack of guidance in the specification, is too broad because it encompasses biological response systems that would not be capable of assessing feeding and/or weight gain, predicting risk, diagnosing obesity and/or energy imbalance. It is not clear what biological response is measured given this definition. Some biological responses, such as measurement of feeding frequency and/or body weight gain (paragraph [0039] of the specification), are predictive of the risk of developing obesity, imbalance in energy homeostasis or disturbance in feeding/weight gain patterns. Given the above-discussed lack of guidance in the literature and the broad definition in the specification of "biological response systems," claim 15 is not enabled as currently recited.

Finally, regarding claims 25 and 29-30, the specification and prior art, only provide guidance regarding measurement of the desacetyl-α-MSH/α-MSH ratio in plasma, and not saliva, sweat, urine, amniotic fluid, cord blood, cerebrospinal fluid, and in vitro cell, organ or tissue sample. Although claim 29 recites "an in vitro cell, organ or tissue sample or whole animal capable of responding to melanocortin peptides," the art does not support the use of such a broad array of tissues even in a case where the tissue is responsive to melanocortins. For instance, while Katsuki et al (cited above) teach that elevated plasma levels of α-MSH are correlated with insulin resistance in obese males, thus support the use of plasma in the instantly claimed methods, Harrold et al. (cited above) teach that elevated hypothalamic levels of AGRP but not α-MSH or POMC may indicate obesity or energy imbalance, thus they do not support the use of hypothalamic tissue in the instantly claimed methods because melanocortins were

unchanged in the hypothalamic tissue of obese rats, in spite of the fact that this tissue may be responsive to melanocortins. Given these teachings, which underscore the state and the unpredictability of the art, the person of skill in the art would need to undergo undue experimentation to establish which tissues recited in the claims could be used in the claimed inventions. In other words, the person of skill in the art, could not rely on the guidance of the literature to fill in the gaps not taught in the specification. For this reason, the claimed methods are not enabled for being carried out in any tissue.

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The reason is given in the paragraph immediately preceding this one, namely the evidence in the literature suggests that hypothalamic tissue would not be useful in the instantly claimed methods, since Harrold et al. that neither α-MSH nor POMC measured in hypothalamic tissue are indicative of obesity or energy imbalance.

Due to the large quantity of experimentation necessary to determine the melanocortins that could be used in the claimed methods and the tissues wherein they could be measured, the lack of direction/guidance presented in the specification and the absence of working examples directed to the same, the complex nature of the invention given the contradictory state and unpredictability of the art (see the discussion above

regarding the state of the art), (the level of skill of those in the art) and the breadth of the claims which fail to recite limitations the melanocortins used or the tissues which would provide useful measurements to carry out the claimed invention, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-11, 14, 16, 17, 18, 19, 20, 23, 25, 29, 31 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Mauri et al. (Horm Res. 1990; 34: 66-70). Mauri et al. teach the measurement of α-MSH and desacetyl-α-MSH in plasma the plasma of women, followed by calculation of the desacetyl-α-MSH/α-MSH ratio (see for example p. 68, right column, 1st paragraph—claims 8-11, 14, 16, 23, 25, 29, 31—the claim is broad and encompasses carrying the assay out in a human, because humans contain a hypothalamus). In addition, the α-MSH and desacetyl-α-MSH were separated via HPLC fractionation and the MSH was measured via a quantitative radioimmunoassay (see p. 67, left column, 2nd and 3rd full paragraphs—claims 17, 18, 19, 20, 34). Note that for the purpose of prior art, the claims are interpreted as the measurement two melanocortin peptides in a sample, calculating the ratio, and comparing the value of the

ratio with a reference value in any patient population and for any purpose (see Rejections under 35 U.S.C. 112, second paragraph).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D. can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth C. Kemmerer

Christina Borgeest, Ph.D.

ELIZABETH C. KEMMERER. PH.D.
PRIMARY EXAMINER